Immunotherapeutic strategies for systemic lupus erythematosus: preliminary analysis and prospective applications

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Abstract

Systemic lupus erythematosus (SLE) is a complex autoimmune disease causing inflammation and tissue damage. Traditional treatments have limitations, prompting exploration of biological therapies.

SLE involves abnormal interplay between innate and adaptive immunity. Impaired clearance of cellular debris and dysfunctional macrophages contribute to autoantibody production. Dendritic cells, particularly plasmacytoid DCs (pDCs), overproduce interferon-α (IFN-α), while B cell activity is heightened with breakdown of tolerance. Cytokines like IL-6 and IL- 23 also play a role.

Belimumab, targeting B-cell activating factor (BAFF), is the first new SLE drug in over 50 years. Saphnelo, an anti-type I interferon receptor antibody, is another recent approval. Several antibody-based therapies are under investigation. Obetiximab targets CD19, while Rituximab (RTX) targets CD20. Obinutuzumab and Ofatumumab are alternatives for RTX-resistant cases. Dapirolizumab pegol (DZP) targets CD40L, and Daratumumab targets CD38. Ustekinumab (anti-IL-12/IL-23) failed phase III trials.

Traditional Chinese Medicine (TCM) options like Rehmannia Six Formula and Artemisinin show promise. Emerging biological therapies include KP-104, a bifunctional complement inhibitor for SLE-associated thrombotic microangiopathy (SLE-TM), and Daxdilimab, targeting pDCs for moderate-to-severe discoid lupus erythematosus (DLE). Bispecific antibody therapy offers exciting possibilities. Rozibafusp alfa, a first-in-class candidate, targets both BAFF and ICOS-L, showing preclinical benefit. It is currently in phase II trials for SLE. Tibulizumab, targeting BAFF and IL-17, has completed phase I trials in other autoimmune diseases. PRV-3279, targeting CD32B and CD79B on B cells, is in phase Ia safety trials.Cell therapy with KYV-101, an anti-CD19 CAR T cell therapy, and Mesenchymal stem cell (MSC) therapy are also being investigated. Precision medicine tailors treatment based on individual characteristics. Omic technologies help identify treatment-sensitive patients.

Despite progress, SLE remains a complex disease. Sirolimus, an immunosuppressant, shows promise in reducing disease activity and improving serological responses. Epigenetics research explores microRNA (miRNA) dysfunction as a potential target. miR-146 and miR-155 are being investigated for their role in SLE. miRNA-based therapies hold promise due to their ease of production and potential for oral administration. Future directions include exploring combination therapies and optimizing clinical trial design for SLE. This review highlights the potential of biological therapies for improving SLE treatment.